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10/693,059

10/23/2003

James McSwiggen

03-465-A (400.136)

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02/03/2009

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EXAMINER

PITRAK, JENNIFER S

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

02/03/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/693,059 | Applicant(s) MCSWIGGEN ET AL. | |
| | Examiner JENNIFER PITRAK | Art Unit 1635 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/31/08.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18 and 20-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18 and 20-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> |

Continuation of Attachment(s) 6). Other: P. Haeberli declaration under 37 CFR 1.132 filed 10/31/08.

DETAILED ACTION

Remarks

Applicant's arguments and Peter Haeberli's declaration under 37 CFR 1.132 have been entered and considered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 18 and 20-33 currently pending and are under examination.

Claim Rejections - 35 USC § 102 - Maintained

The rejection of claims 18 and 20-33 under 35 U.S.C. 102(e) as being anticipated by Fosnaugh and McSwiggen (US2003/0143732) is maintained for the reasons of record. The declaration of Peter Haeberli filed 10/31/2008 is not sufficient to overcome the rejection. The declaration states that Dr. James McSwiggen is an inventor of the currently claimed invention, which was also disclosed in Application No. 10/224,005 (published as US2003/0143732). This fact is not in dispute. Applicant has not shown that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention by another.

Claim Rejections - 35 USC § 103 - Maintained

Claims 18 and 20-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbashir, *et al.* (2001, EMBO J., v.20(23):6877-88, of record, 07/09/2007 IDS), Monia and Cowsert (2000, U.S. Patent 6,033,910), Piekini (1991, Science, v.253:314-7, of record,

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07/09/2007 IDS), and Matulic-Adamic, *et al.* (1999, U.S. Patent 5,998,203, of record, 07/09/2007 IDS). This rejection is maintained for the reasons of record.

Response to arguments

Applicant argues that Elbashir does not teach or suggest a single siRNA molecule having at least two different modifications and that this cannot be remedied by the disclosure of the other cited references because modifications that were commonly known to stabilize antisense molecules against nuclease degradation have been reported to be detrimental to RNAi activity if applied to an siRNA molecule beyond the terminal nucleotides or if at all, by the Elbashir reference. This is not persuasive because Elbashir teaches that siRNAs with 2'-deoxy nucleotides at the end of siRNA strands were functional and suggested that siRNAs with 2'-OMe nucleotides at the end of siRNA strands were also functional, but that fully 2'-deoxy or 2'-methyl-modified siRNAs were less effective at silencing than unmodified or partially modified siRNAs (Figure 4; p.6881, last paragraph; p.6885, left column). Although Elbashir does not demonstrate the use of two different modifications within a single siRNA, Monia teaches the use of two different modifications at the ends of antisense oligonucleotides to increase oligonucleotide stability. One of skill in the art would readily recognize that such dual modification could also be used in the siRNAs of Elbashir. Applicant interprets the disclosure of Elbashir at page 6885, left column, lines 7-13, regarding Figure 4, to indicate that any 2'-O-methyl modification is not at all tolerated in siRNAs. Such interpretation is not agreed to by the Examiner. First, at page 6881, last paragraph, Elbashir states 21-nucleotide (nt) siRNAs with 2-nt 3' overhangs with 2'-deoxy- or 2'-O-methyl-modified strands were examined. Elbashir comments on the results of the 2'-deoxy-end-modified siRNAs and does not comment on the results of the 2'-O-methyl-end-modified siRNAs. Figure 4 shows the successful use of 2'-deoxy-

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modified nucleotides at the ends of siRNA strands and contrasts these end-modified siRNAs with fully 2'-deoxy- and fully 2-methyl-modified siRNAs which have reduced functionality. From this Figure and the discussion at pages 6881 and 6885 (left column), one of skill in the art would recognize that use of 2'-methyl modifications at the ends of siRNAs would likely produce very similar results as shown for 2'-deoxy modifications. The statement on p.6885, "[M]ore extensive 2'-deoxy or 2'-O-methyl modifications reduce the ability of siRNA to mediate RNA," is interpreted by the Applicant to mean that 2'-O-methyl should not be used at all in siRNAs. Examiner disagrees and interprets this phrase in context to mean that both 2'-deoxy- and 2'-O-methyl-modified nucleotides can effectively be used at the ends of the siRNAs, as shown for 2'-deoxy in Figure 4, but not throughout the siRNA.

Applicant then argues that there is no expectation that other known modifications, such as the 2'-F modification of Monia/Pieken and terminal cap moieties of Matulic-Adamic, and known motifs, such as the gapmers of Monia, could be applied to siRNAs. Applicant has provided no evidence to support this contention, but drew an analogy between the instant situation and putting out fires. This is not persuasive because, taken with Elbashir's teaching of modifying siRNA terminal nucleotides, one of skill in the art would reasonably expect that those modifications useful for stabilizing antisense oligonucleotides and ribozymes, could also stabilize siRNAs if incorporated according to the end-only pattern taught by Elbashir.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635

/Tracy Vivlemore/
Primary Examiner, Art Unit 1635